

Docket No.: 21058/0206455-US0  
Intel Corporation  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Tae-Woong KOO et al.

Application No.: 10/814,695

Filed: March 30, 2004

For: SURFACE MODIFICATION OF METALS  
FOR BIOMOLECULE DETECTION USING  
SURFACE ENHANCED RAMAN  
SCATTERING (SERS)

Assignee: Intel Corporation

Confirmation No.: 7238

Art Unit: 1641

Examiner: M. J. Yu

**DECLARATION OF DR. TAE-WOONG KOO UNDER 37 CFR 1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Tae-woong Koo, declares under penalty of perjury under the laws of the United States of America as follows:

(1) I have received a Ph.D. in Mechanical Engineering in 2001 from Massachusetts Institute of Technology. I had been a research scientist at Intel Corporation ("Intel"), where I entered employment in 2001, for four years. My field of research has been the use of optical techniques, especially Raman scattering, for sensitive detection of biological molecules. I have more than a dozen peer-reviewed publications in academic journals, and I have served as a peer-reviewer for multiple academic journals. In 2005, I was promoted to a manager.

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(2) I am familiar with the subject matter and claims of the present application. I am also familiar with the teachings of U.S. Patent 5,384,265 (Kidwell) and U.S. Publication No. US 2003/0199653 A1 (McCormick) cited by the Examiner in the Action of January 24, 2007.

(3) I reviewed the Examiner's rejection in the Action of January 24, 2007, the statement in the Advisory Action of April 3, 2007, and the suggestions in the Interview Summary mailed May 18, 2007, of the interview of May 2, 2007. I agree with the Examiner's statement in the Advisory Action of April 3, 2007, that Example 1 of the specification "discloses comparing the Raman enhancement of the claimed method with the colloids prepared by the titration method, but does not specify that the organic molecules have been attached at the time of comparison nor during the colloidal preparation method." During the interview of May 2, 2007, the Examiner said that Applicants should provide evidence on the record showing that both the metal *and* the organic molecule contribute to producing a Raman signal enhancement that is greater than the enhancement provided by a silver colloid prepared by a titration method as claimed and explained in the specification by filing a Declaration under 37 CFR 1.132. Below, I provide this evidence.

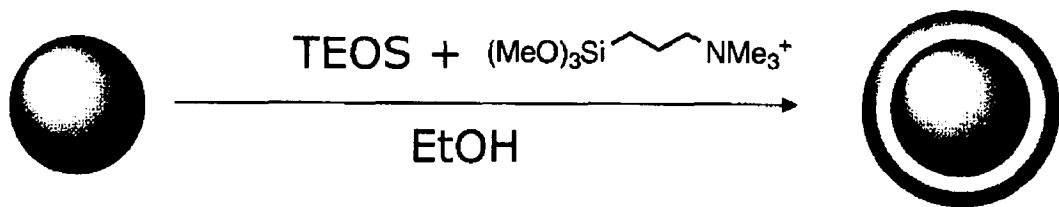
**(4) Experimental data showing strong surface-enhanced Raman signal by surface modification of colloids with organic molecules of trimethylammonium**

**Fabrication Process**

First, silver colloids were fabricated by a method described in the specification of the pending application. Second, a thin layer of silica was deposited onto the silver colloid surface by exposing the colloids to tetraethylorthosilicate (TEOS), and the silica layer was then modified with a trimethylammonium silane to yield surface-modified silver colloids having Raman-enhancing organic molecules (Figure 1).

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**Figure 1.** Process of modifying the surface of silver colloids with trimethylammonium silane

### Experimental Methods

For measurements with the unmodified colloids, the unmodified silver colloids were mixed with the target analyte and lithium chloride similar to the method described in Koo et al, *Appl. Spectrosc.*, 58(12):1401-1407 (2004). For measurements with the surface modified colloids, equimolar mixture of the unmodified colloids and modified colloids were mixed with the target analyte and lithium chloride.

Raman measurements were performed by an in-house built Raman detection unit similar to those described in the specifications.

### Results

Figure 2 shows the comparison of Raman spectra of six different peptides collected by use of the unmodified colloids (left) and the mixture of modified and unmodified colloids (right).

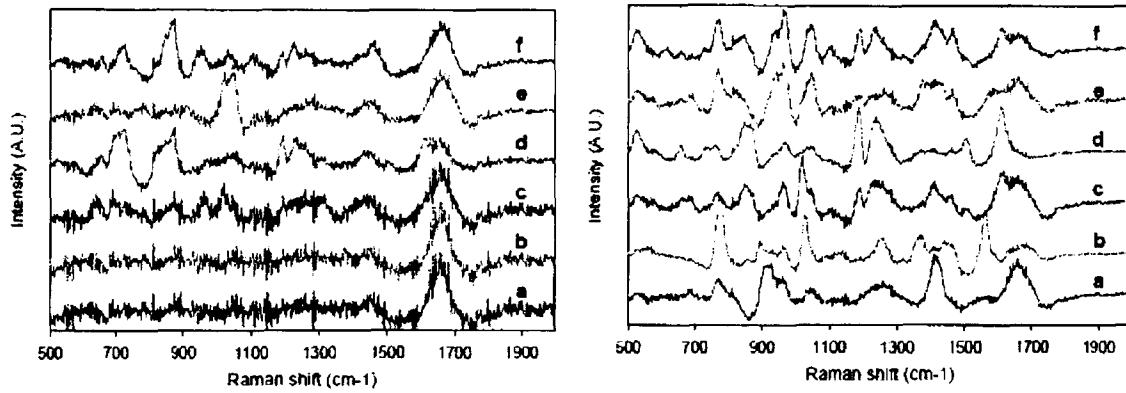
In the left-side figure, acidic peptides, such as hexa-L-aspartic acid (DDDDDD), delta sleep inducing peptide (WAGGDASGE), and beta-amyloid (1-11) (DAEFRHDSGYE) have no or negligible Raman signal. Hexa-L-tyrosine (YYYYYY), buccalin, (GMDSLAFSGGL-NH<sub>2</sub>), and neurotensin (8-13) (RRPYIL) have weak Raman signal with limited features.

In contrast, all six peptides show strong Raman signal with enhanced features when the modified colloids were added to the mixture (right-side figure). Hexa-L-aspartic acid, delta sleep inducing peptide, and beta-amyloid (1-11) show strong peaks that were not observed with unmodified colloids. Hexa-L-tyrosine, buccalin, and neurotensin (8-13) show better quality of data

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(as measured by increased signal-to-noise ratio of the spectra), and additional spectral features not observed with unmodified colloids.



Letter	Name	Sequence	pI
a	Hexa-L-Aspartic Acid	DDDDDD	3.3
b	Delta Sleep Inducing Peptide	WAGGDDASGE	3.6
c	$\beta$ -amyloid (1-11)	DAEFRHDSGYE	4.4
d	Hexa-L-Tyrosine	YYYYYY	5.5
e	Buccalin	GMDSLAFSGGL-NH <sub>2</sub>	6.2
f	Neurotensin (8-13)	RRPYIL	10.8

**Figure 2.** SERS spectra of a set of peptides at concentrations of 100 ng/uL obtained by using unmodified colloids (left) and mixture of modified and unmodified colloids (right)

### Conclusion

The use of metallic colloids having Raman-enhancing organic molecules on the surface of the metallic colloids strongly enhanced the Raman signal of various biological molecules that could not be well observed by metallic colloids not having Raman-enhancing organic molecules on the surface of the metallic colloids.

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(5) I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed at Santa Clara, California, United Stated of America, on this 25<sup>th</sup> day of June 2007.

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Tae-woong Koong